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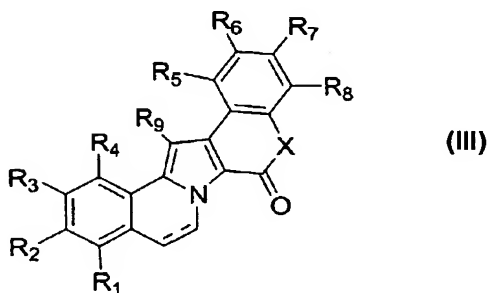
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GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC,
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European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE,

[Continued on next page]

(54) Title: ANTITUMORAL ANALOGS OF LAMELLARINS



(57) Abstract: New lamellarins are provided of the general formula III wherein X is selected from the group consisting of N, O and S; wherein R₁, R₂, R₃, R₄, R₅, R₆, R₇, R₈ and R₉ are each independently selected from the group consisting of H, OH, OR', SH, SR', SO₂R', NHR', N(R')₂, N=R', NHCOR', N(COR')₂, NHSO₂R', NO₂, PO(R')₂, PO₂R', C(=O)H, C(=O)R', CO₂H, CO₂R', OPO(R')₂, OPO₂R', OC(=O)H, OC(=O)R', N=C(R')₂, substituted or unsubstituted C₁-C₁₂ alkyl, substituted or unsubstituted C₁-C₁₂ haloalkyl, substituted or unsubstituted C₂-C₁₂ alkenyl, substituted or unsubstituted C₂-C₁₂ alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl and substituted or unsubstituted heteroaromatic; wherein each of the R' groups is independently selected from the group consisting of H, OH, NO₂, NH₂, SH, CN, halogen, =O, C(=O)H, C(=O)CH₃, CO₂H, C(=O)R', substituted or unsubstituted C₁-C₁₈ alkyl, substituted or unsubstituted C₂-C₁₈ alkenyl, substituted or unsubstituted C₂-C₁₈ alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted C₁-C₁₈ alkoxy, substituted or unsubstituted C₁-C₁₈ aminoalkyl, substituted or unsubstituted C₁-C₁₈ aminoacid, substituted or unsubstituted C₁-C₁₈ thioalkyl, substituted or unsubstituted C₁-C₁₈ alkylsulfinyl, substituted or unsubstituted C₁-C₁₈ alkylsulfonyl; wherein the pairs of groups R₁ and R₂, R₂ and R₃, R₃ and R₄, R₃ and R₉, R₄ and R₉, R₉ and R₅, R₅ and R₆, or R₆ and R₇, R₇ and R₈ may be joined into a carbocyclic or heterocyclic ring system; and the dotted line represents an single or double bond; or a pharmaceutically acceptable salt, derivative, prodrug or stereoisomer thereof.



ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO,
SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM,
GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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Published:

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- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

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INTERNATIONAL SEARCH REPORT

International Application No.

PCT/GB 03/03541

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D491/14 C07D471/14 C07D471/04 A61K31/435 A61P35/00
//(C07D491/14,311:00,221:00,209:00)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	QUESADA AR ET AL: "Polyaromatic alkaloids from marine invertebrates as cytotoxic compounds and inhibitors of multidrug resistance caused by P-glycoprotein" BRITISH JOURNAL OF CANCER, vol. 74, 1996, pages 677-682, XP009019845 UK tables I,II	19,20
Y	ISHIBASHI F ET AL: "Synthesis and structure-activity relationship study of Lamellarin derivatives" JOURNAL OF NATURAL PRODUCTS, vol. 65, pages 500-504, XP002259136 USA cited in the application tables 1,2	19,20
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☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

30 October 2003

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26/03/2004

Name and mailing address of the ISA

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 03/03541

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 97 01336 A (PHARMA MAR SA) 16 January 1997 (1997-01-16) cited in the application claim 1	19,20
Y	--- RIDLEY CP ET AL: "Total synthesis and evaluation of lamellarin alpha 20-sulfate analogues" BIOORGANIC & MEDICINAL CHEMISTRY, vol. 10, 2002, pages 3285-3290, XP002259137 UK table 1	19,20
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INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 03/03541

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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A	<p>ANDERSEN R J ET AL: "METABOLITES OF THE MARINE PROSOBRANCH MOLLUSC LAMELLARIA SP" JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, AMERICAN CHEMICAL SOCIETY, WASHINGTON, DC, US, vol. 107, 1985, pages 5492-5495, XP002218629 ISSN: 0002-7863 cited in the application the whole document</p>	1-16

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 03/03541

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>URBAN S ET AL: "LAMELLARIN-S: A NEW AROMATIC METABOLITE FROM AN AUSTRALIAN TUNICATE, DIDEMNUM SP" AUSTRALIAN JOURNAL OF CHEMISTRY, XX, XX, vol. 49, 1996, pages 711-713, XP000872208 ISSN: 0004-9425 cited in the application the whole document</p>	1-16
A	<p>BANWELL M ET AL: "CONVERGENT TOTAL SYNTHESIS OF LAMELLARIN K" CHEMICAL COMMUNICATIONS, ROYAL SOCIETY OF CHEMISTRY, GB, vol. 23, 1997, pages 2259-2260, XP000867646 ISSN: 1359-7345 the whole document</p>	1-16
A	<p>WO 98 50365 A (BANWELL MARTIN GERHARDT ;UNIV AUSTRALIAN (AU); FLYNN BERNARD LUKE) 12 November 1998 (1998-11-12) cited in the application claim 16</p>	1-16
A	<p>BANWELL MG ET AL: "Assessment of double-barrelled heck cyclizations as a means for construction of the 14-phenyl-8,9-dihydro-6H-1!benzo'4',3':4,5!pyrrolo'2,1-a!isoquinolin-6-one core associated with certain members of the Lamellarin class of marine natural product" AUSTRALIAN JOURNAL OF CHEMISTRY, vol. 52, 1998, pages 755-765, XP009019850 australia the whole document</p>	1-16
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INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 03/03541

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 99 67250 A (BANWELL MARTIN GERHARDT ;UNIV AUSTRALIAN (AU); FLYNN BERNARD LUKE) 29 December 1999 (1999-12-29) cited in the application claim 14 ---	1-16
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INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB 03/03541

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Although claim 19 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compounds.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 03/03541

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